iontophoretic current gradient (7.5 mA) from the same balloon. 5 μCi (2 mg) was given systemically; for local delivery 2.5 μCi (1 mg) was given in each artery. One artery was harvested at 10 min and the second at 4 hr, and radioactivity was assessed in a γ-counter. Studies of binding of ^{125}I-labeled ReoPro® to isolated baboon platelets were also performed.

Results. A small amount of ReoPro® was taken up in balloon-injured brachial arteries by systemic delivery. However, there was about 40-fold higher uptake with both passive and active local delivery at 10 min, with sustained 4- to 14-fold higher retention at 4 hr. Data are cpm/mg tissue for entire artery.

	10 minutes	p vs systemic	4 hours	p vs systemic
Systemic infusion	2.5 ± 3.2	–	6.5 ± 10.5	–
Passive local	97.0 ± 86.6	0.057	26.6 ± 7.0	0.019
Active local	111.9 ± 36.2	0.029	89.7 ± 69.2	0.057

Binding studies showed the number of receptors/platelet was 32,827 ± 4,908. The dissociation constant (K^3) for the affinity-purified, dialyzed ^{125}I-labeled ReoPro® ranged from 2.7 to 9.8 nM (n = 4, 6.2 ± 3.0 nM).

Conclusions. Local delivery whether by passive or active iontophoretic means enhances the deposition and retention of anti-platelet antibodies at sites of arterial balloon injury. Further studies are needed to determine whether active iontophoresis can significantly improve retention, and whether this strategy can reduce platelet recruitment and even neointimal proliferation.

1216-86 Local Delivery of Heparin Into Rabbit Carotid Artery With a Novel Electroporation Catheter

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Background. Effective local delivery of a drug at the site of the arterial lesion has been hampered by its rapid wash-out. We hypothesized that deployment of an electroporation (EP) catheter would strongly favor penetration and retention of the agent into arterial wall and overcome the problem of the drug going into systemic circulation.

Methods. A double balloon EP catheter has been developed where one coiled electrode is placed between the two balloons and a clinical guidewire is used as the second electrode. These are connected to a BTX exponential generator which delivers short pulses. Two methods have been successfully carried out in normal arteries of New Zealand white rabbits (n = 20), where both fluoresceinated and commercial heparin is introduced endoluminally: (i) in the cervically exposed carotids in retrograde mode (n = 14) and (ii) through the femoral artery (n = 6) under fluoroscopic guidance in anterograde mode, *in vivo*, with continuous EKG monitoring. One artery in each pair is pulsed (50 V, 4 × 8 ms pulses) during heparin delivery. The contralateral artery serves as a control and is not pulsed. Arteries are harvested at different time periods for confocal and epifluorescence analysis.

Results. EP does not cause any EKG abnormality. There is no damage to the vessel architecture. Penetration of heparin is deep in the media and adventitia, and retention is longer in the pulsed arteries in contrast to the control samples where a rapid wash-out of heparin is seen.

Conclusions. Local electroporation is very effective both for increased uptake and retention of heparin.

1216-87 Local Drug Delivery: Impact of Substance Characteristics on Drug Transfer Into the Arterial Wall

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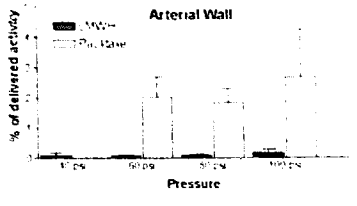
Background. Injection parameters for local drug delivery are frequently determined by studies with marker substances. The pharmacologic properties of the actual drug may influence delivery efficiency and lead to different results.

Methods. Radiolabelled (^{3}H) preparations (5 ml) of the hydrophylic low molecular weight heparin reviparin (LMWH) and the lipophilic taxane paclitaxel were injected into the left anterior descending artery of a freshly explanted porcine heart with the Infusasleeve II. A balloon support pressure of 6 atm and infusion pressures of 40, 60, 80 or 100 psi were used (N = 5 for each group). Arteries along with surrounding myocardium were harvested, homogenized, and activity was measured.

Results are shown in the figure.



For LMWH the concentration in the arterial wall was 20 times higher than in the myocardium. For paclitaxel the factor was 165.

Conclusion. The characteristics of the delivered drug contribute largely to the delivery efficiency. Using identical injection parameters, drug concentrations in the arterial wall were significantly higher for the lipophilic paclitaxel as compared to the hydrophilic LMWH.

1216-88 Results of Prospective Randomized Study of Local Enoxaparin Delivery Versus Systemic Heparinization for NIR Stent Placement

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We postulated that local delivery of enoxaparin via Transport catheter (LE) without full systemic heparinization, prevents stent thrombosis and may have antiproliferative properties reducing restenosis rates. Randomization of 100 pts into LE and systemic heparinization (SH) groups is in progress. LE group received 2,500 U Heparin IV and 10 mg of enoxaparin to the treated site during predilation and SH group 10,000 U Heparin IV, both prior to NIR stent placement. Data (mean ± SD) are presented on 66 pts (48 M, 18 F), age 53.4 ± 8.5 years. 33 pts in LE and 33 in SH group. Baseline ACT's were: 94.6 ± 40.6 in LE group, 120.9 ± 48.9 sec in SH group (NS). After 2,500 U of Heparin IV, ACT was 257.8 ± 168.3 sec, and after enoxaparin ACT was 295.2 ± 168.3 (NS). Final ACT's were: 179.8 ± 106.4 in LE and 360.1 ± 228.9 sec in SH ($p < 0.001$). In SH group reference dia was 2.87 ± 0.38 mm, post stent MLD rose from 0.78 ± 0.33 to 2.53 ± 0.35 mm, and the DS fell from 72.9 ± 11.1% to 9.1 ± 8.6% (both $p < 0.001$). In LE group reference dia was 2.99 ± 0.42 mm, post stent MLD rose from 0.85 ± 0.38 mm to 2.57 ± 0.35, and the DS fell from 71.1 ± 12.6% to 10.7 ± 6.8% (both $p < 0.001$). Acute gain was 1.75 ± 0.41 in SH and 1.72 ± 0.50 mm in LE group (NS). There was no increase in the procedure time when using local drug delivery: 72.1 ± 36.1 min in LE group vs 67.0 ± 35.8 min SH group (NS), however sheaths were removed significantly earlier in LE group: 110.5 ± 49.0 min vs 389.0 ± 113.3 min in SH group ($p < 0.001$). No death, acute MI, emergent CABG, subacute stent closure or groin complications have occurred in either group at the time of procedure and during 30 days of follow-up.

Conclusions. Results of NIR stent deployment were comparable in both groups and reflected substantial acute MLD gain. Effective local drug delivery is suggested since there was no increase of ACT after enoxaparin, and no stent thrombosis had occurred in LE group. LE strategy was associated with earlier ambulation. Six months angiographic follow-up will be available.

1217 Intravascular Ultrasound Doppler Flow and Other New Techniques

Wednesday, April 1, 1998, 3:00 p.m.–5:00 p.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 3:00 p.m.–4:00 p.m.

1217-59 Assessment of Balloon Angioplasty in Intrastent Restenosis With Intra Coronary Ultrasound

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Optimal treatment of restenosis occurring after coronary stenting, is not yet clear even if balloon angioplasty (PTCA) has been demonstrated safe and efficient. The mechanism of balloon angioplasty in intrastent restenosis was studied with serial quantitative coronary angiography (QCA) and intracoronary ultrasound (ICUS) in 43 pts. All pts were dilated with a non compliant balloon inflated at high pressure (>15 atm). QCA and ICUS data were available for all pts at stent implantation (basal), before (control) and after repeat PTCA (final). Minimal lumen diameter (MLD) was assessed with QCA, stent cross-sectional area, reference and stent lumen area and neointimal tissue area (stent area – lumen area) with ICUS.

A significant increase in MLD and lumen CSA was achieved after rePTCA, but lumen size remained at a lower level than at stent implantation. After balloon re-PTCA, there was a significant increase in stent area (7.6 ± 2.9 vs 9.0 ± 2.4 mm) and the neointimal tissue area remained unchanged (3.9 ± 2.3 vs 3.7 ± 2.4).

	Basal (a)	p (a) vs (b)	Control (b)	p (b) vs (c)	Final	p (a) vs (c)
MLD (mm)	2.3 ± 0.5	*	1.1 ± 0.7	*	1.9 ± 0.3	**
Vessel size (mm²)	12.7 ± 3.0	NS	14.5 ± 3.0	NS	15.1 ± 3.2	*
Stent area (mm²)	7.3 ± 3.2	NS	7.6 ± 2.9	**	9.0 ± 2.4	**
Lumen area (mm²)	7.3 ± 3.2	**	2.8 ± 1.4	**	5.4 ± 1.7	
Neotissue (mm²)	-		3.9 ± 2.3	NS	3.7 ± 2.4	

* = p < 0.05 and ** = p < 0.001

We conclude that the mechanism of balloon angioplasty in intrastent restenosis is mainly overexpansion of the stent, most of the neointimal tissue remaining within the stent.

1217-60 The Relationship Between Ultrasound Intensity and Thrombolysis

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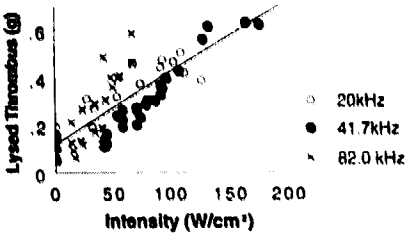
It has been demonstrated that high intensity, low-frequency ultrasound can accelerate thrombolysis. However, the relationship between ultrasound emission characteristics and efficiency of thrombus dissolution is not well understood. We performed ultrasound thrombolysis *in vitro* using a modified ultrasound generator (Misonix sonicator, Microtip probe) at frequencies of 20, 41.7 and 82 kHz and intensities ranging from 0 to 177 W/cm². Reduction of thrombus weight and fibrin release from thrombus were measured.

Result: The relationship between beam intensity and reduction of thrombus weight is shown in the figure below. Fibrin assay showed a similar linear relationship. (20 kHz: R = 0.83, 82 kHz: R = 0.84).



Conclusion: In the range between 20 to 82 kHz there is a linear relationship between ultrasound intensity and thrombus dissolution as assessed by the reduction of thrombus weight and fibrin release. These findings may play an important role in defining the specifications required for a catheter based ultrasound thrombolysis device.

1217-61 Detection of Fibrous cap in Atherosclerotic Plaque by Intravascular Ultrasound Using Color Mapping Technique of Angle-dependent Echo-Intensity Variation

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Background: The thickness of fibrous cap is a major determinant for instability of atherosclerotic plaque. It has been demonstrated that the intensity of intravascular ultrasound (IVUS) backscatter from fibrous tissue is strongly dependent on the ultrasound beam angle. This study investigated the feasibility of a new IVUS color mapping technique representing the angle-dependent echo-intensity variation especially in detecting fibrous cap in atherosclerotic plaque.

Methods: Nineteen formalin-fixed noncalcified human atherosclerotic plaques from necropsy were imaged in vitro with a 25 MHz IVUS catheter. The IVUS catheter was moved coaxially inside the lumen. Then, the degree of change in echo-intensity (maximum minus minimum) was colorized for each portion in the plaques. The plaque segments were also examined histologically by Masson's Trichrome stain.

Results: A clearly-bordered area with large variation in echo-intensity was revealed for each plaque surface in the colorized IVUS image. The thickness (x:mm) of this area was significantly correlated with that of fibrous cap (y:mm) measured from histologic slides, as: $y = 1.0 \times -0.01$ ($r = 0.81$, $p < 0.0001$). The Bland-Altman analysis also supported the reliability of this method (the mean difference = 0.0 ± 0.1 mm).

Conclusions: This novel color mapping technique of the echo-intensity variation in IVUS provided an accurate representation of the thickness of fibrous cap in atherosclerotic plaque. This method may be useful in assessing the plaque instability in patients with acute coronary syndrome.

1217-62 Reproducibility and Biologic Variability of Volumetric Intravascular Ultrasound Measurements

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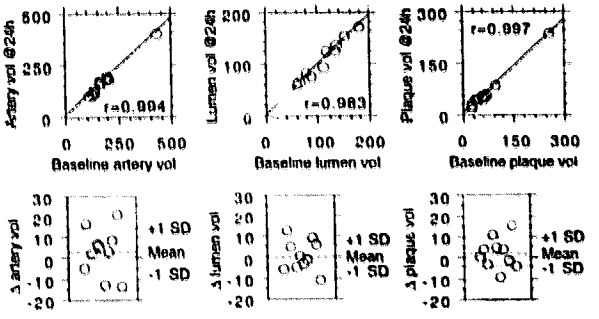
Serial volumetric intravascular ultrasound (IVUS) measurements have been proposed for the detection of atherosclerotic plaque progression and regression. To assess the reproducibility and biologic variability of these measurements, untreated left main coronary arteries in 10 patients were studied 24 hrs apart. All IVUS studies were performed with automatic transducer pullback @ 0.5 mm/sec. An automatic contour detection algorithm was used to measure artery, lumen, and plaque (artery − lumen) volumes (vol, mm³) over 7.2 ± 2.5 mm long segments. Plaque burden (plaque/artery vol) was modest (33 ± 11%).



We Conclude: Serial volumetric IVUS analysis is reproducible, and there is only minor short term biologic variability. Serial volumetric IVUS analysis should prove useful for studying atherosclerosis progression and regression.

1217-63 Novel Multi-Manipulatable Functioned Percutaneous Transluminal Coronary Angioscope

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Background: Clinical use of coronary angioscope (CAS) is limited partly due to good coaxial view cannot be obtained in curved coronary artery. Therefore, we developed a new percutaneous transluminal CAS which has two novel functions (1) good torque control (one to one torque ratio) and (2) slant visual axial tip.

Methods: This angioscopic catheter composed of outer catheter and inner angioscope (1.5 mm, 0.6 mm in diameter, respectively). The inner angioscope is able to not only rotate 360 degrees but also move 50 mm along the coronary artery. The slant visual angle was 30 degrees to design to have the highest visualization success rate. We performed comparative study on visualization capability of new CAS and commercial available conventional monorail type CAS in 10 canine coronary arteries. CAS was inserted into left anterior descending artery (LAD) or circumflex coronary artery (CX) from right femoral artery through 8F guide catheter.

Results: Visualization of whole inner lumen of CX and distal LAD could not be obtained in all cases with conventional CAS. However, good visualization of inner lumen of both proximal and distal LAD and CX were obtained in all cases with new CAS. No complications were occurred during angioscopy. Pathological examination showed no thrombus or intimal exfoliation.

Conclusions: This new CAS is the first one which can observe coronary inner lumen in whole segments completely. This new CAS can remarkably improve the efficacy of angioscopic examination.

1217-64 Volumetric Plaque Quantification by Intravascular Ultrasound: Reproducibility, Variability and Validation

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Background: Intravascular ultrasound (IVUS) visualizes plaque directly and may be used for quantification in interventions; the accuracy of IVUS requires further evaluation.

Methods: In vivo: IVUS imaging (2.9 F, 30 MHz) was performed in 95 coronary segments in 30 pts. (28 m, 2 f) with coronary disease. After pullback #1 (automated, 1.0 mm/sec), the catheter was removed and repositioned for pullback #2. IVUS images were digitized and cross-sections were analyzed visually. Parameters were: Plaque volumen and plaque surface area (vessel surface covered by plaque) within segments (marked by branches). *In*